ORIGINAL ARTICLE

Analysis of colorectal cancer occurrence during surveillance colonoscopy in the dietary Polyp Prevention Trial CME

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Background: Interval colorectal cancer (CRC) occasionally is detected in patients who have recently undergone colonoscopy. Systematic evaluation of CRC detected after colonoscopy could identify ways to improve the quality and the outcome of colonoscopy.

Methods: This study examined cancer diagnoses in the course of the dietary Polyp Prevention Trial, a randomized study of a dietary intervention on recurrence of adenomatous polyps. An algorithm was developed to classify each cancer into one of 4 etiologies: (1) incomplete removal (cancer at the site of previous adenoma), (2) failed biopsy detection (cancer in an area of suspected neoplasia with negative biopsy specimens), (3) missed cancer (large, advanced stage cancer found at a short interval after colonoscopy), or (4) new cancer (small, early stage cancer after a longer time interval).

Results: Of 2079 patients, 13 had cancer detected over 5810 person years of observation (PYO) (2.2 cases/1000 PYO); 7/13 or 53.8% of patients had either a potentially ''avoidable'' cancer or one detectable at an earlier time interval because of incomplete removal (4/13) or missed cancer (3/13).

Conclusions: Interval cancer occurs despite colonoscopy. Improved quality of colonoscopy may have reduced cancer prevalence or resulted in earlier cancer detection in over 50% of prevalent cancers in the dietary Polyp Prevention Trial. (Gastrointest Endosc 2005;61:385-91.)

Colonoscopy can detect colorectal neoplasia, and, through removal of premalignant adenomatous polyps, it can reduce the incidence of colorectal cancer (CRC).[1,2] Because of an approximate 10% recurrence rate per year of adenomatous polyps, patients with this neoplasm are advised to undergo repeated colonoscopy to detect and remove recurrent adenomas.[3] But, despite this benefit of colonoscopy, interval cancers occasionally are detected in patients with a history of recent colonoscopy.

The rate of cancer during follow-up colonoscopy was 0.6/1000 person years of observation (PYO) in the National Polyp Study.[1] Colonoscopy was performed by highly skilled endoscopists at a few select medical centers. In contrast, the CRC risk in 3 community-based polyp prevention trials involving thousands of patients and hundreds of endoscopists was 2.4/1000 PYO.[3] The reasons for the comparatively higher rate of cancer occurrence in these studies is unclear, but the results suggest that the effectiveness of colonoscopy in the larger community, as determined by the rate of cancer incidence, may not be as promising as that indicated by the National Polyp Study.

Only a few studies have attempted to evaluate the reasons for CRC detection in patients who have had a recent colonoscopy. Explanations for these interval cancers include limited depth of insertion relative to eventual cancer diagnosis,[4] biologic factors that lead to rapid tumor progression,[5] and incomplete adenoma removal because of piecemeal polypectomy.[6] Missed lesions, inherent to the performance of colonoscopy, also are a factor.[7-10] One dilemma, often impossible to definitively resolve, is whether an interval cancer is a missed lesion or a new growth.

The dietary Polyp Prevention Trial (PPT) is a randomized, controlled study of the effect of a low-fat, high-fiber, high fruit and vegetable diet on adenomatous polyp recurrence in 2079 patients in 8 centers across the United States. Thirteen patients had cancers detected over 5810 PYO.

The objective of the present study was to review the circumstances surrounding cancer occurrence in the PPT

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0016-5107/2005/$30.00 + 0
PII: S0016-5107(04)02765-8

and to identify factors associated with CRC detection. An algorithm for studying cancer occurrence in patients under colonoscopic surveillance was developed. Systematic evaluation of failed surveillance could identify ways to enhance the quality and the outcome of colonoscopy, and to improve the development of recommendations for intervals for repeat colonoscopic examinations.

Capsule Summary

What is already known on this topic

- Interval colorectal cancer is occasionally detected despite a recent colonoscopy.

What this study adds to our knowledge

- In a large, randomized, dietary intervention for polyp prevention trial, 2.2 cases of interval colorectal cancer per 1000 patient years of observation were noted.
- More than 50% of interval colorectal cancer could be preventable or detected at earlier stage.

PATIENTS AND METHODS

Patients recruited for the PPTwere at least 35 years of age and had one or more histopathologically confirmed colorectal adenomas removed during a qualifying colonoscopy within 6 months before randomization. Exclusion criteria were the following: history of CRC, surgical resection of an adenoma, bowel resection, polyposis syndromes, inflammatory bowel disease (IBD), body weight greater than 150% of recommended weight, use of lipid-lowering drugs, and a medical condition or a dietary restriction that would substantially limit compliance with the dietary intervention. Participants were recruited from academic and community practices in the vicinity of 8 regional clinical centers: Bowman Gray School of Medicine, Winston-Salem, NC), State University of New York at Buffalo (Buffalo, NY), Edward Hines Jr. Veterans Affairs Medical Center (Chicago, Ill), Kaiser Foundation Research Institute (Oakland, Calif), Memorial Sloan-Kettering Cancer Center (New York, NY), University of Pittsburgh (Pittsburgh, Pa), University of Utah (Salt Lake City, Utah), and Walter Reed Army Medical Center (Washington, DC). Patients returned to their usual endoscopist for follow-up colonoscopy at approximately 1 year (T1 colonoscopy) and 4 years (T4 colonoscopy) after randomization. Procedure reports were obtained for any unscheduled endoscopic procedures performed in addition to the protocol-mandated colonoscopy at 1 and 4 years. All patients provided informed consent. The protocol was approved by the institutional review board at each participating institution.

Demographic information; findings at T0 (baseline) colonoscopy; interval to cancer diagnosis; location, size, and stage of cancer; and circumstances of cancer discovery were evaluated for each patient with cancer (Tables 1 and 2). An advanced adenoma was defined as an adenoma with any one of the following: size 1 cm or greater, at least 25% villous elements, or evidence of high-grade dysplasia.[11] Histopathologic findings were interpreted twice in the PPT: once by the local pathologist and once by a PPT pathologist. The present analysis is based on the interpretation of the PPT pathologist (Table 1).

Each cancer occurrence was grouped into one of 4 potential etiologies: incomplete removal, failed biopsy detection, missed cancer, and new cancer (Fig. 1). The category ''incomplete removal'' included cancers that (1) occurred at the site of a previous adenoma and (2) arose in the absence of a suspicion at endoscopy for residual neoplasia. ''Failed biopsy detection'' included cancers that (1) occurred at the site of a lesion previously suspected to be neoplastic and (2) arose in the presence of a suspicion at endoscopy for neoplasia but with multiple procedures and biopsies required for the eventual cancer diagnosis. ''Missed cancer'' included cancers that (1) occurred in a location different from the site of a previous adenoma and (2) were diagnosed within 30 months or less of the most recent colonoscopy (regardless of size or stage), or (3) were diagnosed more than 30 months after a prior colonoscopy and had all features of an advanced cancer (size $\geq$ 2 cm) and advanced stage (III or IV). ''New cancer'' included cancers that (1) occurred in a site different from that of a previous adenoma, (2) were detected more than 30 months after a colonoscopy, and (3) had no features or only one feature of an advanced cancer (large size or advanced stage).

The algorithm was based on the general premise that cancer is unlikely to appear de novo in less than 30 months. That is, based on the natural history of adenoma,[3] it would be unlikely for a small polyp not detectable at colonoscopy to progress to cancer in less than 30 months. Cancers detected within 30 months were considered missed cancers regardless of characteristics. A large and advanced stage cancer detected between 30 and 60 months also was classified as a missed cancer.

A 5th potential etiology for cancer occurrence during surveillance is ''incomplete examination'' (Fig. 1), i.e., a cancer is detected beyond the known furthest extent of colonoscope insertion (e.g., cecal cancer detected after a colonoscopy known to have extended only to the hepatic flexure). Because the PPT required that all colonoscopies be performed to the cecum, the procedures included in the present study were, by definition, examinations in which the endoscopist believed a complete colonoscopy had been performed. Therefore, no cancer was classified as ''incomplete examination'' in the present study.

RESULTS

Of 2079 patients followed in the dietary PPT, 13 had cancers detected over 5810 PYO. This represents a CRC occurrence in 0.63% or 2.2 cases/1000 PYO.

TABLE 1. Characteristics of patients in polyp prevention trial with colorectal cancer detected during surveillance colonoscopy

Case no.	Age at T0	Age at diagnosis	Gender	Family history CRC	Prior adenoma history	No. T0 adenomas	Most advanced adenoma at T0	Largest adenoma size at T0 (cm)	Dysplasia at T0
1	57	58	M	No	No	3	Villous	2.5	High
2	52	53	M	No	Yes	1	Tubular	1.5	Low
3	63	68	M	No	Yes	2	Tubular	0.8	Low
4	63	67	M	No	No	1	TVA	1.5	Low
5	69	70	F	Yes	Yes	1	Tubular	NA	Low
6	69	70	M	No	No	4	Tubular	1.3	High
7	75	79	M	No	No	2	Villous	1.5	Low
8	69	73	F	No	No	2	TVA	<1.0	High
9	74	79	F	No	No	1	Tubular	0.5	Low
10	69	74	M	No	No	3	Tubular	0.7	High
11	69	70	M	No	No	3	Tubular	1.0	Low
12	74	76	M	No	No	1	Tubular	0.2	Low
13	72	73	M	No	No	1	Tubular	NA	High

T0, Baseline colonoscopy for eligibility to enroll in the Polyp Prevention Trial; *CRC,* colorectal cancer; *TVA,* tubulovillous adenoma; NA, not available.

Demographic information; polyp findings at the T0 colonoscopy; time interval to cancer diagnosis; location, size, and stage of the detected CRC; and circumstances of cancer discovery are presented in Tables 1 and 2.

The average age at diagnosis was 70.0 years (range 53-79 years), and 76.9% of the patients (10/13) were men. Only one patient had a family history of CRC, and 3 had a history of an adenoma before the PPT index (baseline) T0 colonoscopy. At baseline colonoscopy, 53.8% (7/13) had two or more adenomas and 69.2% (9/13) had an advanced adenoma. Of those with advanced adenoma, 54.5% (6/11) had an adenoma 1 cm or greater in size, 30.8% (4/13) had an adenoma with villous elements, and 38.5% (5/13) had an adenoma with high-grade dysplasia. Baseline adenoma size was missing for two patients.

The average interval from prior colonoscopy to CRC detection was 22.0 months (range 2-44 months). The majority of the patients, 69.2% (9/13), had cancer detected during a scheduled, per protocol colonoscopy at year 1 (4/13) or year 4 (5/13). Only one of these patients had symptoms (right upper quadrant abdominal pain, anorexia, and weight loss) before diagnosis (Case 6). The remaining 4 patients had cancer detected during an unscheduled colonoscopy. The cancers were located in the rectosigmoid (6/13), the splenic flexure (2/13), the transverse colon (1/13), the hepatic flexure (2/13), the ascending colon (1/13), and the cecum (1/13); 53.8% (7/13) were proximal to or within the splenic flexure (Fig. 2). Five cancers, or 38.5% (5/13), were located in the cecum or at one of the flexures. The sizes listed for measured cancers averaged 1.9 cm (range 0.5-3.3 cm); two cancers were of undetermined size. Of all cancers, 61.5% (8/13) were early stage (I or II).

All cancers were analyzed with the algorithm (Fig. 1) as follows: 4 incomplete removal, 3 failed biopsy detection, 3 missed cancers, and 3 new cancer cases. Illustrative examples for each of these cancer categories are provided in Table 3. The classification for cancers detected at the T1 colonoscopy was either missed cancer or incomplete removal, whereas most of the cancers detected at the T4 colonoscopy were classified as new cancers. Failed biopsy detection delayed the diagnosis of cancer by a mean of 15.7 months (8, 16, and 23 months). Three of 4 assessed as incomplete removal occurred in the rectosigmoid region. All 3 cancers associated with failed biopsy detection also were in the sigmoid colon. The 3 missed cancers were located in the flexures or the cecum, whereas the 3 new cancers were all located proximal to or within the splenic flexure.

Of the patients with a diagnosis of cancer, 53.8% had a potentially ''avoidable'' reason for failed or delayed detection (missed lesion [3/13] or incomplete removal [4/13]) and 46.2% were determined to have an unavoidable reason for failed cancer detection (failed biopsy detection [3/13] or new cancer [3/13]).

DISCUSSION

Colonoscopy is considered the criterion standard procedure for detection of colorectal neoplasia, but it is not

TABLE 2. Characteristics of CRCs detected during surveillance colonoscopy

Case no.	T0—CRC interval (mo)	Interval from most recent colonoscopy (mo)	When CRC detected	Why CRC detected	Location of CRC	CRC size (cm)	TNM stage	UICC/AJCC stage	Assessment
1	14	14	T1	T1 routine	Sigmoid	0.8	T1 Nx Mx	I	Incomplete removal
2	12	12	T1	T1 routine	Rectum	3.3	T3 N1 M0	III	Incomplete removal
3	54	39	T4	T4 routine	Ascending colon	2.5	T4 N1 M0	III	Incomplete removal
4	44	44	44 m after T0	Skipped T1 examination	Sigmoid	2.5	T1 N0 M0	I	Incomplete removal
5	12	12	T1	T1 routine	Cecum	2.0	T2 N0 M0	I	Missed cancer
6	14	14	T1	T1 symptoms	Hepatic flexure	3.0	T3 N2 M1	IV	Missed cancer
7	45	30	T4	T4 routine	Splenic flexure	3.0	T2 N0 Mx	I	Missed cancer
8	53	35	T4	T4 routine	Splenic flexure	0.5	T1 N0 M0	I	New cancer
9	52	41	T4	T4 routine	Transverse colon	1.3	T1 N0 M0	I	New cancer
10	54	32	T4	T4 routine	Hepatic flexure	2.0	T1 N0 M0	I	New cancer
11	8	8	8 m after T0	Cautery effect	Sigmoid	0.5	T3 N0 M0	II	Failed biopsy detection
12	23	3	23 m after T0	Colovesical fistula	Sigmoid	NA	Tx Nx M1	IV	Failed biopsy detection
13	16	2	16 m after T0	Prominent fold	Sigmoid	NA	T3 N2 MX	III	Failed biopsy detection

T0, Baseline colonoscopy for eligibility to enroll in the Polyp Prevention Trial; *CRC,* colorectal cancer; *NA,* not available.

perfect. Cancers occur despite colonoscopy. There is a paucity of studies of the circumstances of CRC occurrence in the setting of prior colonoscopy, and there is no consensus as to the optimal method for evaluating such cancers.

Haseman et al.[4] identified 47 cancers that occurred within 3 years of a colonoscopy. Given the limited number of poorly differentiated tumors and the low likelihood of hereditary nonpolyposis colorectal cancer (HNPCC), they concluded that most of the cancers were missed at the prior colonoscopy. Gorski et al.[5] identified 29 cancers in patients who had colonoscopy performed by colorectal surgeons within the previous 5 years.[5] Because the interval from prior colonoscopy was short (mean 23 months) and the tumors were large (mean size in cecum 4.4 cm, mean size in other locations 2.4 cm), Gorski et al.[5] concluded that the majority of the cancers were missed lesions. Both groups of investigators acknowledged, however, that the growth rate of tumors is variable and that it is difficult to determine whether a cancer might have been ''detectable'' at the initial colonoscopy. At face value, large, advanced cancers detected a short time after colonoscopy likely represent missed cancers, whereas small, early stage cancers detected at a longer interval after colonoscopy are more likely to be new cancers.

Many factors were incorporated in the development of our algorithm (Fig. 1) for analysis of interval cancers, including the extent of examination (depth of insertion), time interval since prior colonoscopy, location of prior adenoma(s), results of prior biopsies, residual neoplasia, and the size and the stage of the CRC.

Based on this analysis, 7 of 13 patients, or 53.8%, had cancers that were potentially avoidable or amenable to earlier detection because of incomplete removal of an advanced adenoma or of a missed cancer; the remainder had cancers that were unavoidable because of failed biopsy detection or new cancer. Lessons can be learned from both the avoidable and unavoidable groups.

Cancers categorized as ''incomplete removal'' highlight deficiencies in technique and assessment of the completeness of adenoma excision. It has been shown that CRC may develop from incompletely excised large adenomas.[12] Three of our 4 patients with cancer had an adenoma 1 cm or greater in size at the baseline examination in the area of subsequent CRC. Adenomas with advanced features are more likely to progress to adenocarcinoma, and, therefore, their complete removal

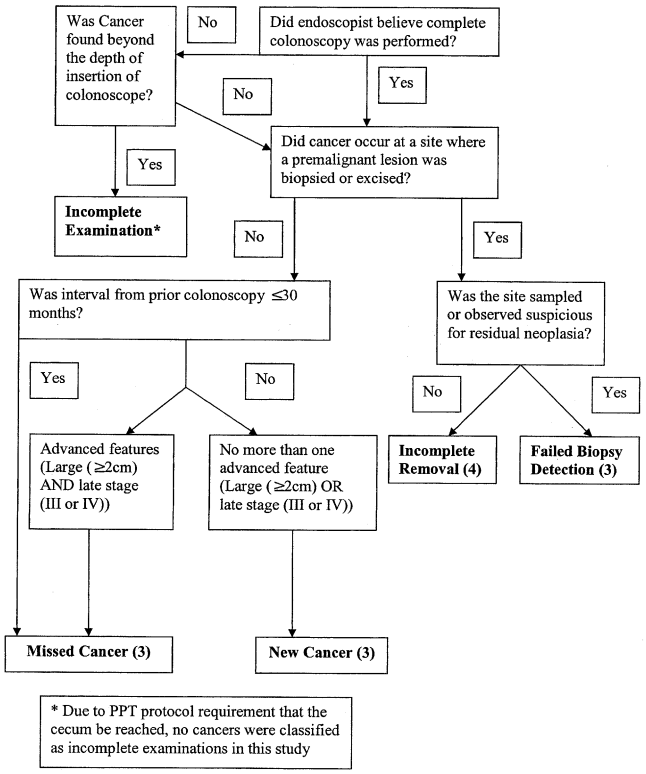

Figure 1. Algorithm for cancer occurrence during surveillance colonoscopy.

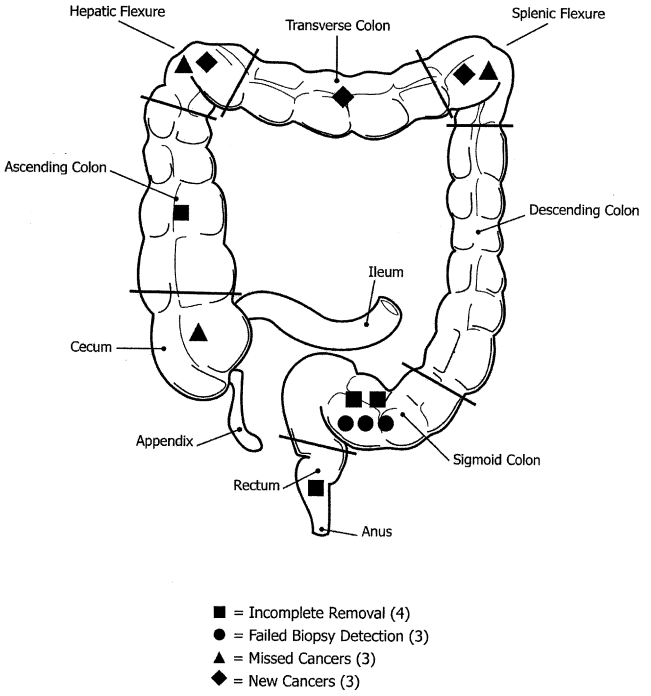

Figure 2. Location of CRC occurrence by etiology.

must be assured. In the Funen Adenoma Follow-up Study, 60% (6/10) of patients with cancer identified over a period of 6 to 48 months after colonoscopy had a previous adenoma within the area of CRC formation, and, in 50% (3/6) of these cases, piecemeal polypectomy technique had been used.[6] Thus, the ''incomplete removal'' category highlights the importance of complete excision of advanced adenomas. Potential improvements include accelerated follow-up surveillance in patients with advanced adenomas that are difficult to remove (piecemeal polypectomy, uncertainty about totality of excision, or equivocal histopathologic margins) and the liberal use of the India ink tattoo[13] to target surveillance of advanced lesions.

The ''missed cancer'' cases highlight human error in performing colonoscopy. The missed cancers in the present study were relatively large (2 cm, 3 cm, 3 cm) and were detected within 30 months of a prior colonoscopy. They were located in the cecum, the hepatic flexure, and the splenic flexure, respectively. One factor that potentially contributed to missed cancers is failure to intubate the cecum despite the belief of the endoscopist that the cecum had been reached. Several studies have stressed the importance of formally documenting cecal landmarks for assurance of a complete examination.[14,15] In the guidelines offered by the U.S. Multi-Society Task Force on Colorectal Cancer on quality in the technical performance of colonoscopy, visualization of the lips of the ileocecal valve, and the appendiceal orifice were endorsed as the best landmarks to ensure and to verify cecal intubation.[16] Additional evaluation of the proximal colon, e.g., by liberal use of radiographic imaging when cecal landmarks cannot be verified, should be encouraged. Also, meticulous examination of the flexures, because lesions frequently are missed in these areas,[17] and adequate time for withdrawal (at least 6-10 minutes) should be emphasized to ensure a quality examination.[16]

Although the missed cancer potentially involves human error, it is important to emphasize that technical limitations of colonoscopy are a contributing factor. Meticulous examination does not guarantee detection of polyps and advanced lesions.[10] Even when the endoscopist was likely thorough and knew that a subsequent colonoscopy was to be performed, 12% to 13% of polyps 6 to 9 mm in size and up to 6% of polyps 1 cm or larger in size were missed in tandem colonoscopy studies.[7,9] A study of virtual colonoscopy further emphasizes the limitations of colonoscopy in detecting lesions.[10]

Some occurrence of cancer during surveillance is unavoidable. ''Failed biopsy detection'' cases highlight deficiencies in endoscopic sampling and histopathologic assessment of nonpolypoid cancers. Factors contributing to this circumstance include negative biopsy results for folds or strictures that appear neoplastic, uncommon cancers (adenocarcinoma arising in a crypt, with no polypoid component; e.g., Case 13), thermal artifact that prevents visualization of the intraepithelial cells (''cautery effect,'' e.g., Case 11), and an extraluminal mass compressing the lumen in the area of a diverticulum (Case 12); all of

TABLE 3. Illustrative examples of etiology of cancer occurrence in the Polyp Prevention Trial

Incomplete removal	
Case 1	Advanced 25-mm villous adenoma removed at baseline (T0) colonoscopy from mid sigmoid colon; T1 colonoscopy revealed an 8-mm moderately differentiated adenocarcinoma in same region.
Failed biopsy detection	
Case 11	Adenomatous polyp with margins obscured by thermal artifact preventing cancer diagnosis.
Case 12	Extraluminal mass seen at baseline T0 colonoscopy compressing lumen in area of a diverticulum; biopsy specimens interpreted as "hemorrhagic chronic ulcer base with inflammatory cellular atypia, dense plasmacytic infiltrates, and dysplastic cells"; mass not seen on subsequent examinations with negative biopsy specimens; patient presented with colovesical fistula and metastatic disease.
Case 13	Prominent sigmoid fold seen at T0 colonoscopy with negative biopsy specimens; multiple interval procedures with negative biopsy specimens; concern for malignancy despite negative biopsy specimens led to surgical excision of an adenocarcinoma in a crypt without significant polypoid portion.
Missed cancer	
Case 6	"Cecum" was intubated at T0 colonoscopy, which revealed small tubular adenomas; 1 y later, patient experienced right upper quadrant abdominal pain with CT evidence of a right-sided mass; T1 colonoscopy revealed a 3-cm obstructing adenocarcinoma at hepatic flexure (stage IV).
New cancer	
Case 8	Two tubulovillous adenomas detected at T0 colonoscopy (12 cm, 40 cm); no polyp found at T1 colonoscopy; T4 colonoscopy detected 5 mm adenocarcinoma in splenic flexure (stage I).

these were seen at baseline T0 examinations. In the present series, ''failed biopsy detection'' delayed the diagnosis of cancer by a mean of 15.7 months. However, in all of these cases, the concern of the endoscopist remained despite the indeterminate biopsy specimens. These cases emphasize the importance of astute and experienced endoscopic observation, as well as the limitations of relying solely on histopathologic assessment. Radiographic imaging with CT and surgical excision of suspect strictures, even with negative biopsy specimens, should be considered when these difficult clinical problems are encountered.

Interobserver variability in the histopathologic assessment of adenomatous tissue is another concern, because intervals for follow-up surveillance colonoscopy are guided by the interpretation of resected polyps.[3] Five of the 13 cancers in the present series were interpreted as high-grade dysplasia by the central pathologist but were read as low (2 cases) or moderate grade (1 case) dysplasia, or the degree of dysplasia was not described (2 cases), by the local pathologist. There is variability in the determination of advanced adenoma status with regard to histopathologic type (villous vs. tubular) and degree of dysplasia.[18] In a study of the histopathologic interpretation of colorectal polyps by pathologists in community practice, 35% of the tubular adenomas were designated tubulovillous or villous, whereas the tubulovillous or villous adenomas were labeled tubular in only 2% of cases.[19] Thus, when formally studied in the community, overdiagnosis of villous histopathology was more common than underdiagnosis, which would lead to a recommendation for a more aggressive instead of less aggressive surveillance interval. It should be emphasized that the PPT protocol mandated more frequent surveillance than would be done in normal clinical practice.

The category ''new cancer'' used in the present study may be explained by biologic variability in the time interval of the adenoma–carcinoma sequence. The progression from adenoma to carcinoma generally is thought to span 10 years,[20] but instances of more rapid progression are described.[21,22] A biologically aggressive but small lesion not seen at colonoscopy could progress to invasive cancer within a few years. The ''new cancer'' cases detected in the present study were found an average of 36 months (range 32-41 months) after a prior colonoscopy.

For a cancer to be considered ''new,'' the criterion used in the current study was a time interval of more than 30 months between diagnosis and the prior colonoscopy. All of the new cancers were early stage lesions, and the prognosis for patients with these malignancies, therefore, was good. Two of the 3 patients with new cancers had an advanced adenoma at the baseline examination. Patients with advanced adenoma have a 3- to 4-fold increase in risk for subsequent CRC.[12] They also are at increased risk for subsequent advanced adenomas.[3] These cases emphasize the importance of adhering to the current surveillance guideline of repeat colonoscopy within 3 years in patients with advanced adenoma.[3]

The present study has certain limitations. Our algorithm is based on a small number of cases of CRC reviewed retrospectively. It uses arbitrary definitions (e.g., cancer

diagnosed within 30 months or less was classified as ''missed''). To validate our algorithm, it would be helpful if it were applied to cancers detected in other clinical trials and under other circumstances. Surveillance colonoscopy in the PPT was performed at a predefined interval of 1 and 4 years by protocol. Because surveillance is performed at varying intervals in the community, it will be important to evaluate our approach to cancer occurrence in other settings where variable surveillance intervals are used. Because patients with IBD, HNPCC, and prior CRC were excluded, the results of the current study are not applicable to these patient groups. Finally, our assessment of avoidable vs. unavoidable cancer detection is based on reasonable clinical judgment and analysis of available information. It is never certain that a cancer detected at any point in time was or was not detectable at some time before its discovery. Given the consequences for patients of failed detection of CRC, systematic evaluation of cancer occurrence after colonoscopy is necessary for improvement of patient outcome. Improved quality of colonoscopy may have reduced cancer prevalence or resulted in earlier cancer detection in over 50% of cancers in the PPT.

REFERENCES

1. Winawer SJ, Zauber AG, Ho MN, O'Brien MJ, Gottlieb LS, Sternberg SS, et al. Prevention of colorectal cancer by colonoscopic polypectomy. The National Polyp Study Workgroup [see comments]. N Engl J Med 1993;329:1977-81.
2. Mandel JS, Church TR, Bond JH, Ederer F, Geisser MS, Mongin SJ, et al. The effect of fecal occult-blood screening on the incidence of colorectal cancer. [letter; comment]. N Engl J Med 2000;343:1603-7.
3. Schoen RE. Surveillance after positive and negative colonoscopy examinations: issues, yields, and use. Am J Gastroenterol 2003;98: 1237-46.
4. Haseman JH, Lemmel GT, Rahmani EY, Rex DK. Failure of colonoscopy to detect colorectal cancer: evaluation of 47 cases in 20 hospitals. [see comments]. Gastrointest Endosc 1997;45:451-5.
5. Gorski TF, Rosen L, Riether R, Stasik J, Khubchandani I. Colorectal cancer after surveillance colonoscopy: false-negative examination or fast growth? Dis Colon Rectum 1999;42:877-80.
6. Jorgensen OD, Kronborg O, Fenger C. The Funen Adenoma Follow-up Study. Incidence and death from colorectal carcinoma in an adenoma surveillance program. Scand J Gastroenterol 1993;28:869-74.
7. Rex DK, Cutler CS, Lemmel GT, Rahmani EY, Clark DW, Helper DJ, et al. Colonoscopic miss rates of adenomas determined by back-to-back colonoscopies [see comments]. Gastroenterology 1997;112:24-8.
8. Bensen S, Mott LA, Dain B, Rothstein R, Baron J. The colonoscopic miss rate and true one-year recurrence of colorectal neoplastic polyps. Polyp Prevention Study Group. Am J Gastroenterol 1999;94:194-9.
9. Hixson LJ, Fennerty MB, Sampliner RE, McGee D, Garewal H. Prospective study of the frequency and size distribution of polyps missed by colonoscopy. J Natl Cancer Inst 1990;82:1769-72.
10. Pickhardt PJ, Choi JR, Hwang I, Butler JA, Puckett ML, Hildebrandt HA, et al. Computed tomographic virtual colonoscopy to screen for colorectal neoplasia in asymptomatic adults. [see comment]. N Engl J Med 2003;349:2191-200.
11. Schatzkin A, Lanza E, Corle D, Lance P, Iber F, Caan B, et al. Lack of effect of a low-fat, high-fiber diet on the recurrence of colorectal adenomas. Polyp Prevention Trial Study Group [see comments]. N Engl J Med 2000;342:1149-55.
12. Atkin WS, Morson BC, Cuzick J. Long-term risk of colorectal cancer after excision of rectosigmoid adenomas [see comments]. N Engl J Med 1992;326:658-62.
13. Nizam R, Siddiqi N, Landas SK, Kaplan DS, Holtzapple PG. Colonic tattooing with India ink: benefits, risks, and alternatives [review]. Am J Gastroenterol 1996;91:1804-8.
14. Rex DK. Still photography versus videotaping for documentation of cecal intubation: a prospective study. Gastrointest Endosc 2000;51: 451-9.
15. Marshall JB, Brown DN. Photodocumentation of total colonoscopy: how successful are endoscopists? Do reviewers agree? Gastrointest Endosc 1996;44:243-8.
16. Rex DK, Bond JH, Winawer S, Levin TR, Burt RW, Johnson DA, et al. Quality in the technical performance of colonoscopy and the continuous quality improvement process for colonoscopy: recommendations of the U.S. Multi-Society Task Force on Colorectal Cancer. Am J Gastroenterol 2002;97:1296-308.
17. Rex DK, Rahmani EY, Haseman JH, Lemmel GT, Kaster S, Buckley JS. Relative sensitivity of colonoscopy and barium enema for detection of colorectal cancer in clinical practice [see comment]. Gastroenterology 1997;112:17-23.
18. Terry MB, Neugut AI, Bostick RM, Potter JD, Haile RW, Fenoglio-Preiser CM. Reliability in the classification of advanced colorectal adenomas. Cancer Epidemiol Biomarkers Prev 2002;11:660-3.
19. Rex DK, Alikhan M, Cummings O, Ulbright TM. Accuracy of pathologic interpretation of colorectal polyps by general pathologists in community practice. Gastrointest Endosc 1999;50:468-74.
20. Winawer SJ, Fletcher RH, Miller L, Godlee F, Stolar MH, Mulrow CD, et al. Colorectal cancer screening: clinical guidelines and rationale [see comments] [published errata appear in Gastroenterology 1997; 112: 1060 and 1998;114:625]. Gastroenterology 1997;112:594-642.
21. Jarvinen HJ, Mecklin JP, Sistonen P. Screening reduces colorectal cancer rate in families with hereditary nonpolyposis colorectal cancer [see comments]. Gastroenterology 1995;108:1405-11.
22. Lanspa SJ, Jenkins JX, Cavalieri RJ, Smyrk TC, Watson P, Lynch J, et al. Surveillance in Lynch syndrome: how aggressive? Am J Gastroenterol 1994;89:1978-80.

Received August 2, 2004. For revision October 12, 2004. Accepted November 16, 2004.

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Presented at the American Society for Gastrointestinal Endoscopy Meeting, May 15-20, 2004, New Orleans, Louisiana (Gastrointest Endosc 2004;59:AB110).

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